



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,518	12/12/2001	Asaph Aharoni	4916US	5379

7590 07/14/2004
Trask Britt & Rossa
P O Box 2550
Salt Lake City, UT 84110

EXAMINER

SAIDHA, TEKCHAND

ART UNIT	PAPER NUMBER
----------	--------------

1652

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/857,518	Applicant(s) AHARONI ET AL.	
	Examiner Tekchand Saidha	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 and 43 is/are pending in the application.
- 4a) Of the above claim(s) 1-18, 22-33 and 35-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-21, 34 and 43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☒ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1652

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all future correspondence regarding this application should be directed to Group Art Unit 1652.

2. The Preliminary Amendment filed June 25, 2003, incorporating a substitute copy of the sequence listing is acknowledged.

3. ***Election***

Applicant's election without traverse of Group II (claims 19-21, 34 & 43 corresponding to SEQ ID Nos. 6 and 31) is acknowledged [see page 1 of Applicant's response to restriction, May 17, 2004]. However, on page 2 of their response, Applicants traverse the sequence selection and point out the supposed errors in the restriction requirement. Specifically Applicants point out that the Commissioner has partially waved the requirements of 37 C.F.R. 1.141 and will permit a reasonable number of sequences to be examined even though they might normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. See, MPEP 2434. Under this policy, up to 10 independent and distinct nucleotide are to be examined in a single application without restriction. Therefore, requiring the Applicants to select only two sequences for examination is against the Office's own policy. Consequently, Applicants should be allowed to select 10 sequences for separate searches and consideration.

In response, the lack of unity requirement pertaining to nucleotide sequences according to MPEP 2434 is reproduced as follows :

>UNITY OF INVENTION - NUCLEOTIDE SEQUENCES

Under 37 CFR 1.475 and 1.499 et seq., when claims do not comply with the requirement of unity of invention, i.e., when the claimed subject matter does not involve "one or more of the same or corresponding special technical features," 37 CFR 1.475(a), an additional fee is required to maintain the claims in the same application. 37 CFR 1.476(b).

The Commissioner has decided *sua sponte* to partially waive 37 CFR 1.475 and 1.499 et seq. to permit applicants to claims up to ten (10) nucleotide sequences which do not have the same or corresponding special technical feature, without the payment

Art Unit: 1652

of an additional fee. The PCT permits inventions which lack unity of invention to be maintained in the same international application for payment of additional fees. Thus, in international applications, for each group for which applicant has paid additional international search and/or preliminary examination fees, the PTO has determined that up to four (4) such additional sequences per group is a reasonable number for examination. Further, claims directed to the selected sequences will be examined with claims drawn to any sequence combinations which have a common technical feature with the selected sequences. Nucleotide sequence encoding the same protein are considered to satisfy the unity of invention standard and will continue to be examined together.

As can be seen from the Commissioner's directive, the reference is to international application for search and preliminary examination report and not to US applications. Further, the USPTO has determined the number of nucleotide sequences to be searched in international Application be four (4) and not ten (10). In the instant US case, this is not applicable because this is not an international application, it is the national stage of the international application, and the sequences in question are amino acid sequences of SEQ ID Nos. 6 and 31, and are not nucleotide sequences as argued by the Applicants.

Finally, 37 C.F.R. 1.499 states that, if the Examiner finds that a national stage application lacks unity of invention under 37 C.F.R. 1.475, the Examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted. Thus, the determination of lack of unity is proper under the PCT treaty.

The lack of unity determination is still deemed proper and is therefore made FINAL.

Applicants' selection of SEQ ID NO: 6 [alcohol acyl transferase, strawberry] and SEQ ID NO: 31 [alcohol dehydrogenase], in spite of being distinct inventions, is granted in order to be consistent with lack of unity requirement made in the previous Office Action.

Art Unit: 1652

4. Claims 19-21, 34 & 43 corresponding to SEQ ID Nos. 6 and 31, are pending and under consideration in this examination.

5. **Claims withdrawn** :

Claims 1-18, 22-33, 35-40 (fully) & 43 (in-part) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed, at least in-part.

6. ***Priority***

Acknowledgment is made of Applicants' claim for priority based on an application filed in EPO on 12/02/1998 [98204018.0]. No certified copy of this document has been received. A certified copy of this document will be required in order to determine and receive priority benefit of December 2, 1998. Until that time Applicants are deemed to a priority date of December 02, 1999, the filing date of PCT/NL99/00737, for prior art purposes.

7. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

8. ***Claim Objections***

Claims 19-21, 34 & 43 are objected for reciting non-elected subject matter. In response to this Office Action Applicants are required to amend the claims deleting non-elected elected subject matter.

9. ***Claim Rejections - 35 USC §112*** (first paragraph)

Written description

Claims 19-21, 34 & 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 19-21, 34 & 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of polypeptide molecules with either SEQ ID NO: 6 or 31 or polypeptide having the limitations of 'a fragment of any size' or a polypeptide having the amino acid sequence which is 30%, 50% or 70% identical to SEQ ID NO: 6 or a polypeptide that is 55% identical to SEQ ID NO: 31 (claims 19-21, 34 & 43).

Claims 19-21, 34 & 43 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO: 6 or 31 including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NO: 6 or 31 and fragments of SEQ ID NO: 6 or 31 that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO: 6 or 31 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the function of all the polypeptide sequences derived from SEQ ID NO: 6 or 31, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of functions and with the potentiality of generating many different antibodies. Therefore many functionally unrelated polypeptides are encompassed

Art Unit: 1652

within the scope of these claims. The specification discloses two full length functional species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

10. ***Enablement***

Claims 19-21, 34 & 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an alcohol acyl transferase of SEQ ID NO: 6 and an alcohol dehydrogenase of SEQ ID NO: 31 (both from strawberry), does not reasonably provide enablement for any alcohol acyl transferase having 30%, 50% or 70% identity to SEQ ID NO: 6; or any alcohol dehydrogenase having 55% identity to SEQ ID NO: 31; or any fragments thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of alcohol acyl transferases and alcohol dehydrogenases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the

Art Unit: 1652

ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequences of alcohol acyl transferase and alcohol dehydrogenase of SEQ ID NO: 6 & 31 respectively.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of any alcohol acyl transferase with 30%, 50 or 70% identity to the enzyme of SEQ ID NO: 6, or all modifications of any alcohol dehydrogenase with 55% identity to the enzyme of SEQ ID NO: 31, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting alcohol acyl transferase or alcohol dehydrogenase activity; (B) the general tolerance of alcohol acyl transferase or alcohol dehydrogenase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any alcohol acyl transferase or alcohol dehydrogenase residues with an expectation of obtaining the desired biological function; and (D) the specification

Art Unit: 1652

provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including alcohol acyl transferase or alcohol dehydrogenase with an enormous number of amino acid modifications of the of SEQ ID Nos: 6 & 31. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of alcohol acyl transferase or alcohol dehydrogenase having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

11. ***Claim Rejections - 35 USC § 112*** (second paragraph)

(a) Claims 19-21, 34 & 43 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19, 34 and 43 recite the phrase 'involved in the biosynthetic pathways for aliphatic and/or aromatic ester production in fruit'. The claims are indefinite because it is not clear which of two enzymes of SEQ ID NO: 6 and 31 are involved in both or one (and/or) aliphatic and aromatic ester production in fruit. Suitable amendment and/or clarification is required to overcome this rejection.

Claims 20-21 are included in the rejection for failing to correct the defect present in the base claim(s).

Art Unit: 1652

(b) Claim 43 recite the phrase 'diagnostic kit'. The claim is indefinite because it is unclear how a kit comprising a polypeptide of SEQ ID NO: 6 or 31 is sufficient in diagnosing 'volatile aliphatic and/or aromatic ester compound'. Suitable amendment and/or clarification is required to overcome this rejection.

12. ***Claim Rejections - 35 USC §102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 19-21 & 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Accession No. Q23943 [01 Jan, 1998].

Claims 19-21 & 43 recite the phrase "or a fragment thereof" referring to isolated polypeptide of SEQ ID NO: 6. There is no limitation present in the claims which would restrict the size of the claimed polypeptide fragment. Di- and tri- peptides are well known in the art of molecular biology and chemistry and are encompassed by the scope of these claims. Therefore, the claims are anticipated by fragment in the disclosed accession no., which has fragments larger than di- or tri-peptide(s) and which match Applicants' SEQ ID NO: 6, and therefore anticipates the claims.

13. Claim 34 is rejected under 35 U.S.C. 102(a) as being anticipated by Accession No. T12571 [23 July, 1999].

Claim 34 recites the phrase "or a fragment thereof" or 55% homology referring to isolated polypeptide of SEQ ID NO: 31. There is no limitation present in the claims

Art Unit: 1652

which would restrict the size of the claimed polypeptide fragment. Di- and tri- peptides are well known in the art of molecular biology and chemistry and are encompassed by the scope of these claims. Therefore, the claims are anticipated by fragment in the disclosed accession no., which has fragments larger than di- or tri-peptide(s) and which match Applicants' SEQ ID NO: 31 as well a homology of 55%, and therefore anticipates the claims.

14. Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Accession No. S28045 [1993].

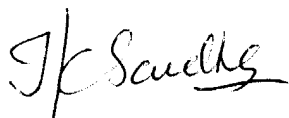
Claim 34 recites the phrase "or a fragment thereof" referring to isolated polypeptide of SEQ ID NO: 31. There is no limitation present in the claims which would restrict the size of the claimed polypeptide fragment. Di- and tri- peptides are well known in the art of molecular biology and chemistry and are encompassed by the scope of these claims. Therefore, the claims are anticipated by fragment in the disclosed accession no., which has fragments larger than di- or tri-peptide(s) and which match Applicants' SEQ ID NO: 31, and therefore anticipates the claims.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (571) 272-0940. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group in the Technology Center is 703 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 571 272-1600.



Tekchand Saidha
Primary Examiner, Art Unit 1652
Recombinant Enzymes, E03A61 Remsen Bld.
400 Dulany Street, Alexandria, VA
Telephone : (571) 272-0940
July 12, 2004